

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 18465-0041	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2005/028829	International filing date (<i>day/month/year</i>) 15 August 2005 (15.08.2005)	Priority date (<i>day/month/year</i>) 13 August 2004 (13.08.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).
 2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 19 June 2007 (19.06.2007) Authorized officer <div style="text-align: center; font-weight: bold;">Yolaine Cussac</div> e-mail: pt11.pct@wipo.int
---	--

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
WILLIAM L. WARREN
SUTHERLAND ASBILL & BRENNAN LLP
999 PEACHTREE STREET, NE
ATLANTA, GA 30309-3996

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 18465-0041		Date of mailing (day/month/year) 24 MAY 2007
FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/US05/28829	International filing date (day/month/year) 15 August 2005 (15.08.2005)	Priority date (day/month/year) 13 August 2004 (13.08.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(8): C12N 5/00(2006.01),5/06(2006.01) USPC: 435/325,377,405		
Applicant UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 20 April 2007 (20.04.2007)	Authorized officer Taeyoon Kim Telephone No. 571-272-0700
--	--	---

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/28829

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/28829

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-73</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-73</u>	NO
Industrial applicability (IA)	Claims <u>1-73</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-73 lack novelty under PCT Article 33(2) as being anticipated by Fisk et al.

Claims are drawn to a method of differentiating pluripotent mammalian cells by contacting with a PI3-kinase inhibitor and TGFβ family member to induce endodermal differentiation, and a composition of cells having endodermal marker expression, and a composition having a cell culture medium, a PI3-kinase inhibitor and a member of TGFβ family.

Fisk et al. teach a method to induce human embryonic stem cells (pluripotent cells) into endodermal lineage (pancreatic islet cells) by using factors for differentiation such as activin A (TGFβ family member) and wortmannin (PI3-kinase inhibitor) (see Table 1 in page 7). Fisk et al. also teach the markers for endodermal differentiation of human ES cells such as SOX17 and HNF4a (see Table 2). Expression of certain lineage markers listed in the current invention would have been inherently achieved by the method of Fisk et al. Thus, the reference anticipates the claimed subject matter.

Claims 1-73 lack an inventive step under PCT Article 33(3) as being obvious over Fisk et al. in view of Hori et al. and Kumar et al. Fisk et al. teach the use of wortmannin and activin for induction of endodermal lineage of human embryonic stem cells. Fisk et al. do not teach the use of LY294002 or BMP. Hori et al. teach a method of differentiating embryonic stem cells into endodermal lineage such as insulin-producing tissue using LY294002 (PI3-kinase inhibitor) in the culture medium. Since wortmannin and LY294002 are known in the art as PI3-kinase inhibitor, it would have been obvious to replace wortmannin with LY294002 since they are art-recognized equivalents.

Similarly, it would have been obvious for a person of ordinary skill in the art to replace activin A with other TGFβ family member such as BMP since they are art-recognized equivalents.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 1-73 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.